What is claimed is:

1. A method of conferring donor CDR binding affinity onto an antibody acceptor variable region framework, comprising:

(a) constructing a population of altered antibody variable region encoding nucleic acids, said population comprising encoding nucleic acids for an acceptor variable region framework containing a plurality of different amino acids at one or more acceptor framework region amino acid positions and donor CDRs containing a plurality of different amino acids at one or more donor CDR amino acid positions;

(b) expressing said population of altered variable region encoding nucleic acids, and

(c) identifying one or more altered variable regions having binding affinity substantially the same or greater than the donor CDR variable region.

2. The method of claim 1, wherein said one or more altered variable regions are identified by comparing the relative binding of said altered variable regions to said donor CDR variable region.

3. The method of claim 1, wherein said one or more altered variable regions are identified by measuring the binding affinity of said altered variable regions.

4. The method of claim 1, wherein said one or more altered variable regions are identified by measuring the association rate (kon) or disassociation rate (koff) of said altered variable regions.

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5 ~~6~~. The method of claim 1, wherein said acceptor variable region framework is a light chain variable region framework.

6 ~~7~~. The method of claim 1, wherein said framework amino acid positions are located in framework region 1, framework region 2, framework region 3 or framework region 4.

7 ~~8~~. The method of claim 1, wherein said donor CDR amino acid positions is ~~located~~ in CDR1, CDR2 or CDR3.

8 ~~9~~. The method of claim 1, wherein said one or more amino acid positions in said acceptor framework region is selected by differences in amino acid identity between corresponding positions in donor and acceptor framework regions.

9 ~~10~~. The method of claim 1, wherein said one or more amino acid positions in said ~~acceptor~~ framework region is selected as being a canonical framework residue.

10 ~~11~~. The method of claim 1, wherein said one or more amino acid positions in said acceptor framework region is selected as being exposed to solvent.

11 ~~12~~. The method of claim 1, wherein said one or more amino acid positions in said acceptor framework region is selected by a characteristic within the group consisting of being proximal to a CDR, predicted to contact the opposite domain in the V_L-V_H interface, lack of relatedness to the donor framework amino acid position at that position and predicted to modulate CDR activity.

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13. The method of claim 1, wherein said one or more amino acid positions in said donor CDR isselected as being a CDR residue as defined by Kabat

14. The method of claim 5, wherein said altered variable regions are coexpressed with a light chain variable region.

15. The method of claim 6, wherein said altered variable region is coexpressed with a heavy chain variable region.

16. A method of simultaneously grafting and optimizing the binding affinity of a variable region binding fragment, comprising:

(a) constructing a population of altered heavy chain variable region encoding nucleic acids comprising an acceptor variable region framework containing donor CDRs and a plurality of different amino acids at one or more framework region and CDR amino acid positions;

(b) constructing a population of altered light chain variable region encoding nucleic acids comprising an acceptor variable region framework containing donor CDRs and a plurality of different amino acids at one or more framework regions and CDR amino acid positions;

(c) coexpressing said populations of heavy and light chain variable region encoding nucleic acids to produce diverse combinations of heteromeric variable region binding fragments, and

(d) identifying one or more heteromeric variable region binding fragments having affinity substantially the same or greater than the donor CDR heteromeric variable region binding fragment.

16 ~~17~~. The method of claim 15 ~~16~~, wherein said one or more heteromeric variable region binding fragments are identified by comparing the relative binding of said heteromeric variable region binding fragments to said donor CDR heteromeric variable region binding fragment.

17 ~~18~~. The method of claim 15 ~~16~~ wherein said one or more heteromeric variable region binding fragments are identified by measuring the binding affinity of said heteromeric variable region binding fragments.

18 ~~19~~. The method of claim 15 ~~16~~, wherein said one or more heteromeric variable region binding fragments are identified by measuring the association rate (kon) or disassociation rate (koff) of said heteromeric variable region binding fragments.

19 ~~20~~. The method of claim 15 ~~16~~, wherein said framework amino acid positions are located in framework region 1, framework region 2, framework region 3 or framework region 4.

20 ~~21~~. The method of claim 15 ~~16~~, wherein said donor CDR amino acid positions is located in CDR1, CDR2 or CDR3.

21 ~~22~~. The method of claim 15 ~~16~~, wherein said one or more amino acid positions in said acceptor framework region is selected by differences in amino acid identity between corresponding positions in donor and acceptor framework regions.

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22 ~~23~~. The method of claim ~~16~~ 15, wherein said one or more amino acid positions in said acceptor framework region is selected as being a canonical framework residue.

23 ~~24~~. The method of claim ~~16~~ 15, wherein said one or more amino acid positions in said acceptor framework region is selected as being exposed to solvent.

24 ~~25~~. The method of claim ~~16~~ 15, wherein said one or more amino acid positions in said acceptor framework region is selected by a characteristic within the group consisting of being proximal to a CDR, predicted to contact the opposite domain in the V_L-V_H interface, lack of relatedness to the donor framework amino acid position at that position and predicted to modulate CDR activity.

25 ~~26~~. The method of claim ~~16~~ 15, wherein said one or more amino acid positions in said donor CDR is selected as being a CDR residue as defined by Kabat.

26 ~~27~~. A method of optimizing the binding affinity of an antibody variable region, comprising:

(a) constructing a population of antibody variable region encoding nucleic acids from a parent variable region encoding nucleic acid, said population comprising two or more CDRs containing a plurality of different amino acids at one or more CDR amino acid positions;

(b) expressing said population of variable region encoding nucleic acids, and

(c) identifying one or more variable regions having binding affinity substantially the same or greater than the parent variable region.

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28. The method of claim 26, wherein said one or more variable regions are identified by comparing the relative binding of said variable regions to said parent variable region.

29. The method of claim 26, wherein said one or more variable regions are identified by measuring the binding affinity of said variable regions.

30. The method of claim 26, wherein said one or more variable regions are identified by measuring the association rate (kon) or disassociation rate (koff) of said variable regions.

31. The method of claim 26, wherein said variable region is a heavy chain variable region.

32. The method of claim 26, wherein said variable region is a light chain variable region.

33. The method of claim 26, wherein said two or more CDRs are selected from the group consisting of CDR1, CDR2 or CDR3.

34. The method of claim 26, wherein said one or more amino acid positions in said two or more CDRs is selected as being a CDR residue as defined by Kabat.

35. The method of claim 26, wherein said variable regions are coexpressed with a light chain variable region.

36. The method of claim 31, wherein said variable regions are coexpressed with a heavy chain variable region.

~~37~~ 36. The method of claim ~~27~~ 26, wherein said antibody variable region is selected from the group consisting of native, grafted, altered and optimized variable regions.

~~38~~ 37. A method of optimizing the activity of a catalytic antibody variable region, comprising:

(a) constructing a population of heavy chain variable region encoding nucleic acids from a parent heavy chain variable region encoding nucleic acid, said population comprising two or more CDRs containing a plurality of different amino acids at one or more CDR amino acid positions;

(b) constructing a population of light chain variable region encoding nucleic acids from a parent light chain variable region encoding nucleic acid, said population comprising two or more CDRs containing a plurality of different amino acids at one or more CDR amino acid positions;

(c) coexpressing said population of heavy and light chain variable region encoding nucleic acids containing said two or more CDRs having said plurality of different amino acids at one or more CDR positions to produce diverse combinations of heteromeric variable region catalytic fragments, and

(d) identifying one or more heteromeric variable regions having optimized catalytic activity compared to said parent catalytic antibody variable region.

~~39~~ 38. The method of claim ~~38~~ 37, wherein said one or more heteromeric variable regions are identified by comparing the relative catalytic activity of said heteromeric variable regions to said parent variable region.

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40. The method of claim 38, wherein said one or more heteromeric variable regions are identified by measuring a substrate association rate (kon), a substrate disassociation rate (koff), substrate binding affinity, a transition state binding affinity, a turnover rate or a Km.

41. The method of claim 38, wherein said two or more CDRs are selected from the group consisting of CDR1, CDR2 and CDR3.

42. The method of claim 38, wherein said one or more amino acid positions in said two or more CDRs is selected as being a CDR residue as defined by Kabat.